

SEGA CLINICAL TRIAL PROTOCOL

PROTOCOL NUMBER	HSC-MS-17-0436	
PROTOCOL TITLE	SEGA - Sedation versus General Anesthesia for Endovascular Therapy in Acute Ischemic Stroke – a Randomized Comparative Effectiveness Trial.	
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PROTOCOL SYNOPSIS

<p>Title</p>	<p>SEGA: Sedation versus General Anesthesia for Endovascular Therapy in Acute Ischemic Stroke – a Randomized Comparative Effectiveness Trial.</p>
<p>Study Purpose</p>	<p>Background: Endovascular therapy (EVT) with stent retrievers improve functional outcome in acute stroke patients. Although both are routinely performed as usual care during EVT, controversy remains regarding the optimal type of anesthesia during EVT – general anesthesia (GA) vs. sedation (CS). Retrospective case-control studies found an association between better clinical outcomes with the latter. However, one small, single-center randomized trial suggested no significant differences in early outcomes.</p> <p>Primary Objective: To estimate overall treatment benefit (improvement in disability) among acute ischemic stroke patients that are randomized to GA compared with CS during endovascular therapy.</p> <p>Secondary Objectives: Assess safety (as measured by incidence of symptomatic intracranial hemorrhage); rates of EVT procedural complications, reperfusion; and quality of life.</p>
<p>Design</p>	<p>Multicenter, randomized, comparative effectiveness trial with un-blinded caregivers but blinded assessors (PROBE – Prospective Randomized Outcome Blinded Endpoint).</p>
<p>Study Population Overview</p>	<p>260 total acute ischemic stroke patients with proximal intracranial arterial occlusions treated with endovascular therapy within 16 hours of symptom onset. Patients must not require intubation for any clinical indication. Arterial occlusion must be demonstrated by either CT-angiogram (CTA) or MR-angiogram (MRA).</p>
<p>Intervention</p>	<p>Time of randomization is study time=0. Patients will be randomized 1:1 to receive during endovascular therapy either:</p> <ol style="list-style-type: none"> 1) General anesthesia (balanced for equal randomization into intravenous vs. inhalational) or 2) Sedation <p>Both GA and CS delivered and managed by anesthesiologist.</p>
<p>Primary Outcome</p>	<p>Independent functional outcome as measured by the modified ordinal Rankin Scale (mRS) at 90 days assessed by study personnel blinded to treatment.</p>
<p>Secondary Outcomes</p>	<ol style="list-style-type: none"> 1) Dichotomized mRS at 90 days (0-2 vs 3-6) 2) Safety as measured by rates of symptomatic intracerebral hemorrhage within 24-36 hours after endovascular therapy. 3) Angiographic reperfusion defined as modified TICI score \geq 2b. 4) Peri-procedural complications. 5) Difference in 24-36-hour NIHSS scale. 6) Proportion of independent functional outcome at 90 days in GA patients treated with inhalational vs. intravenous medications. 7) Difference in quality of life at 90-days.

<p>Study Duration</p>	<p>Total trial duration: 24 ± 4 months</p> <ol style="list-style-type: none"> Enrollment – approximately 18 months with 6 months of data-monitoring and statistical analysis Patient participation - 90 days
<p>Statistics</p>	<ul style="list-style-type: none"> Planned number of sites (US + international): 10-15. Sample size: 260 patients randomized 1:1 (130 per group). Final analysis uses a Bayesian approach to obtain odds ratio (OR) of good functional outcome at 90-days. Bayesian prior assumes treatment equipoise and uses a neutral, informative prior (OR=1.0; 95% credible intervals of 0.3-3.0). Trial success is defined as a >80% posterior probability that GA is superior (OR >1.0 of 90-day mRS) to CS.
<p>Assessments</p>	<ul style="list-style-type: none"> Baseline: History & physical exam; vital signs; laboratory tests; non-contrast CT head, arterial vessel imaging – CTA or MRA, NIHSS, pre-stroke mRS, home medications. Endovascular Procedure: Continuous vital signs (Blood pressure, pulse, oxygen saturation, PETCO₂ in general anesthesia [GA] patients); anesthesia medications; monitor for device-specific malfunction and serious adverse events; cross-over (e.g., CS to GA). 24-36 hours post EVT: Non-contrast head CT or MRI brain as per local usual care; NIHSS 7-days or discharge (whichever occurs first): Vital signs, physical examination, mRS, NIHSS, Blinded assessment of mRS and NIHSS; Stroke etiology. 90 ± 15 days: Blinded assessment of mRS and Quality of Life; Stroke etiology.
<p>Significance</p>	<p>Data generated will inform the optimal anesthesia management of EVT-treated ischemic stroke patients and would be expected to result in significant change of medical practice.</p>